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14. ABSTRACT In this study, 433 women with invasive breast cancer who had >5 axillary lymph nodes removed were followed for the development of arm lymphedema. Participants completed a baseline interview and subsequent interviews at 6-9 month intervals. Lymphedema was identified through self-report and through measurement of arm volume. Slightly more than half of participants reported arm swelling (n=228; 52.7%). Measured arm volume excess of >10% comparing the surgery-side to the opposite arm was identified in 73 women (16.9%). For both self-reported and measured lymphedema, risk was increased among women with greater body mass. For measured lymphedema only, risk was increased among current smokers and reduced among women in the highest category of recreational physical activity. Our results suggest that maintaining normal body mass, abstaining from smoking, and regular recreational physical activity should be investigated further as prevention strategies for lymphedema, particularly for lymphedema that progresses to more severe disease.

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Lymphedema, epidemiology, risk factors

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INTRODUCTION

Lymphedema of the arm is a common, yet dreaded consequence of breast cancer treatment that can result in substantial functional impairment and distress in affected women. Some aspects of cancer treatment such as axillary surgery and radiation are commonly believed to increase risk of lymphedema. However, other potentially modifiable characteristics or behaviors that may also influence risk of this condition have not been well-studied. In this study, we examined whether modifiable factors, including body weight, physical activity, smoking, and breast reconstruction, are associated with the occurrence of arm lymphedema among women treated for breast cancer. Eligible women were aged 21-74 years of age and residents of King County, Washington at the time of breast cancer diagnosis. They were identified through a population-based cancer registry as having been diagnosed with a first primary invasive breast cancer from October 2002- July 2004. The incidence and timing of arm swelling was assessed using physical measures (arm volume) and self-report of symptoms at a baseline interview and at follow-up interviews conducted throughout the study.

BODY

Research Accomplishments associated with tasks outlined in the Statement of Work are as follows:

Task 1. Develop Plan for Initial and Follow-up Interviews and Measurements, Months 1-3.

All of these tasks have been performed.

a. Final IRB approval will be obtained.

IRB approval was obtained from the Fred Hutchinson Cancer Research Center and from the DOD.

b. Tracking system will be created to track patient contacts, recruitment, and interviews.

The tracking system for this study was developed.

c. Cohort ascertainment through the CSS tumor registry will be initiated.

The full study cohort has been ascertained, and consists of 443 eligible women who completed a baseline interview.

d. Enrollment questionnaire will be developed, piloted and finalized.

The enrollment questionnaire was developed, piloted and finalized, and all enrollment interviews completed.

e. *Interviewer will be trained on study procedures, measurement, and interview administration.*

Interviewer training on all study procedures, including measurement and interview administration, was completed.

Task 2. Subject Recruitment and Initial Data Collection, Months 4-18

a. Potential study subjects will be contacted, and physician notification will be performed.

These procedures have been completed, with a final study cohort of 443 women. The first set of contacts with physicians and study subjects occurred after all Human Subjects approvals were

obtained in May, 2003. As of December, 2006, we had identified 641 eligible women. The status of the 641 women in the study is as follows:

Deceased, before contacted:	10
Physician refusal:	29
Study subject refusal:	159
Subjects contacted, enrollment interview complete:	**443**

b. Participant enrollment interviews and initial measurements will be conducted.
We have completed 443 enrollment interviews. One woman was later found to be ineligible (due to removal of <5 lymph nodes), and an additional nine were excluded from our analyses because they had had bilateral mastectomy and lymph node surgery, so that comparison of measured arm volume between the surgery side and unaffected side was not possible. Thus, the final study cohort was comprised of 433 women.

c. Follow-up questionnaires will be developed, piloted and finalized.
The first, second, and third follow-up questionnaires have been developed and finalized.

d. Data management and programming to create analytic data files for the enrollment questionnaire and arm measurement data will be performed.
These tasks have been completed, and preliminary data from the enrollment questionnaire and arm measures were presented at the DOD Era of Hope meeting in June, 2005.

Task 3. Follow-up Interviews and Data Collection, Months 10-45
a. Follow-up interviews and measurements will be conducted.
Follow-up interviews have been completed. We conducted 423 first follow-up interviews, 408 second follow-up interviews, and 316 third follow-up interviews. Interviewing was completed in December, 2006. Arm measurement was performed each time a woman was interviewed.

b. Data management and programming to create analytic data files from the follow-up questionnaires and repeat arm measurement databases will be performed.
This work has been completed.

c. Identification of women with lymphedema by arm volume measures, and comparison with self-report.
These tasks have been completed. By self-report, slightly more than half of the study participants reported arm swelling (n=228; 52.7%). Lymphedema (defined as a 10% increase in measured arm volume of the surgery-side relative to the nonsurgery-side arm) was identified in 73 women. Sixty (82.2%) of the 73 women with lymphedema based on measurement reported arm swelling, and, of these, all but 6 perceived swelling before the increase in volume was measured. Of the 205 women who did not report arm swelling at any interview, a 10% volume excess was measured among 13 (6.3%).

Task 4. Data Analysis and Report Writing, Months 37-48.
The time period for data analysis and report writing was lengthened through a no-cost extension to this project.

a. Preliminary analyses to compare risk factors of interest among women with and without lymphedema.
Our preliminary analyses have been completed. Our initial set of preliminary analyses was restricted to the baseline interview and arm measurement data, and was presented at the 2005 DOD Era of Hope meeting.

Using the full data set of baseline and follow-up interviews, we also conducted extensive preliminary analyses of the arm measurement data to assess the impact of varying the definition of lymphedema according to the level of absolute volume increase (measured in milliliters) and the level of percentage volume increase. Our preliminary analyses led us to conclude that an absolute volume increase of 200 ml. was reasonably repeatable over time and between interviewers. A percentage volume increase of 10% appeared similarly robust in our population, and offered an advantage over an absolute volume increase in that it was more likely to be independent of body weight.

Preliminary analyses of risk factors for lymphedema defined by self-report vs. measured volume excess identified some differences based on the outcome definition. Therefore, we chose to continue on in our final data analyses with two separate sets of analyses: one examines risk factors for lymphedema among women with self-reported arm swelling, while the second examines risk factors for lymphedema defined as a 10% increase in measured arm volume. As noted above, the preliminary analyses led us to choose a percentage, rather than absolute, increase in arm volume as the most appropriate outcome definition for measured arm volume.

b. Final data analyses will be performed (mos 45-48).
The final data analyses are described in more detail in the attached draft manuscript. We used Cox regression with time since surgery as the time scale for these analyses. Breast cancer treatments were examined as time-dependent variables, and all relative risks were adjusted for time since surgery. We examined the relative risk of lymphedema (identified by self-reported arm swelling, or by a 10% increase in measured arm volume) associated with: baseline demographic characteristics; aspects of breast cancer treatment; personal characteristics at the time of breast cancer diagnosis; and potentially modifiable characteristics, including breast reconstruction, body mass index after cancer diagnosis, cigarette smoking, and physical activity.

c. A final report and initial manuscript will be prepared (most 45-48).
Our draft manuscript is attached as an appendix. This manuscript will be finalized and submitted for publication.

KEY RESEARCH ACCOMPLISHMENTS

- 443 women enrolled in the study; study was later restricted to 433 eligible women.
- First follow-up interviews conducted on 423 women.
- Second follow-up interviews conducted on 408 women.
- Third follow-up interviews conducted on 316 women.
- Preliminary data analysis conducted and reported at the DOD Era of Hope meeting in June, 2005.
- Final data analyses conducted.
- Manuscript describing study findings is in the final stages of preparation.

REPORTABLE OUTCOMES

Preliminary results were reported as a poster presentation and an oral presentation at the DOD Era of Hope Meeting in June 2005 (see abstract in Appendix).

A manuscript reporting the results of this research project is under development, and is submitted as an Appendix.

CONCLUSIONS

Relatively little research has been conducted on the etiology or prevention of lymphedema, yet many women are affected with this condition after treatment for breast cancer. Our findings suggest that restraining from cigarette smoking, maintenance of normal (i.e., not overweight or obese) body mass, and participation in regular recreational physical activity should be investigated further as prevention strategies for lymphedema, particularly for lymphedema that develops some time after cancer treatment or progresses to more severe disease. These behaviors should be further investigated in randomized trials and in observational cohort studies. Such future studies should be designed to enroll patients before cancer treatment is initiated, use objective measures for determination of lymphedema, and be of sufficient size to allow the assessment of both moderate and severe disease.

REFERENCES

None

APPENDICES / BIBLIOGRAPHY

1. An abstract presented at the 2005 DOD Era of Hope meeting is attached.
2. A draft manuscript describing the results of this research project is attached.
3. The following personnel were paid from this project over the entire study period. Please note that in most cases, several names are listed for the same role on the project. This is due to normal personnel turnover in the department during the course of the project as well as specialization of tasks resulting in more than one person undertaking tasks originally budgeted for one person.

   PI: Mary Anne Rossing, PhD
   Co-PI: Kathleen E. Malone, PhD
   Biostatistician: Richard Jacke, Mei Tang
   Project Coordinator: Cecilia O'Brien, Anne Oswald, Diane Setterholm
   Programmer: Kay Byron, Dante del Pilar
   Research Project Interviewer: Jean Jue, Charlotte Palmberg, Camille Taylor, Elaine Tipton, Penny Walden
   Program Assistant: Julie Bittner, Carolyn Burns, Carol Ure
   CSS Technician: C. Schubert (the Cancer Surveillance System (CSS) shared resource was budgeted as an other expense but charged as a direct personnel expense).

RISK FACTORS FOR LYMPHEDEMA IN BREAST CANCER SURVIVORS

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Lymphedema of the arm is a common, yet dreaded consequence of breast cancer treatment that can result in substantial functional impairment and distress. While axillary surgery and radiation treatment are known risk factors for lymphedema, few other characteristics that may influence risk have been studied. Through this research, we will assess whether modifiable factors, including body weight, physical activity, smoking, and breast reconstruction, influence risk of arm lymphedema.

We are conducting a prospective study in a cohort of women aged 21-74 years diagnosed with a first primary invasive breast cancer from October 2002- July 2004. Eligible women have undergone axillary dissection as part of their cancer treatment, and are identified through a population-based cancer registry in Washington State. The occurrence of lymphedema is assessed using physical measures and self-report at regular intervals throughout this four-year study. Arm circumference is measured at 1.5-inch intervals from hand to axilla, and these measures are converted to arm volume. Each time they undergo arm measurement, women also complete questionnaires detailing and updating information on the exposures of interest and potential confounding factors.

Results presented here are based on the baseline questionnaires and measurements of the first 340 women enrolled in the study. Women were enrolled 5-28 months after their initial breast cancer diagnosis (median, 10 months), and 4-28 months after their axillary lymph node surgery (median, 9 months). Seven women who had had bilateral breast cancer and axillary dissection and 1 woman who declined measurement were excluded from subsequent analyses. At interview, 121 women (36.5%) reported that they had experienced swelling of the surgery-side arm for two weeks or longer, and 108 reported current swelling. For 48 women (14.5%), the calculated volume of the surgery-side arm was > 200 ml larger than the contralateral arm. This included 21 (9.5%) of the women who reported no current swelling and 27 (25.0%) of the women who reported current swelling. Increasing body mass was associated with lymphedema identified either by self-report or by calculated arm volume. Relative to women with a body mass index (BMI) < 25, the odds ratios and 95% confidence intervals for lymphedema based upon self-report and arm measurement, respectively, among women with a BMI > 30 were 1.6 (0.9-2.9) and 4.5 (2.0-10.4).

Future analyses in this study cohort will assess changes in arm volume over time and relationships with treatment and lifestyle factors. As increasing numbers of women with breast cancer survive their illness, identifying evidence-based strategies to minimize the long-term consequences of treatment, such as lymphedema, is increasingly important.

The U.S. Army Medical Research and Materiel Command under DAMD17-02-1-0387 supported this work.

Modifiable Risk Factors for Lymphedema among Breast Cancer Survivors

DRAFT

Introduction

Lymphedema of the arm is one of the most dreaded consequences of breast cancer treatment. Although published estimates vary widely, recent reviews suggest that lymphedema may develop in 20-25% of breast cancer patients. Physical problems resulting from lymphedema include loss of motion, pain, weakness, repeated infections, and disfiguring swelling. Psychological consequences include anxiety, depression, sexual dysfunction, and social avoidance. Management is difficult, and available treatment options are cumbersome and often ineffective.

Although axillary surgery and radiation therapy are recognized risk factors for lymphedema, little is known about other characteristics or behaviors that may influence risk. In this study, we assessed the occurrence of lymphedema in a cohort of women whose treatment for breast cancer included axillary surgery with at least 5 lymph nodes removed. We examined associations with breast cancer treatment and other, potentially modifiable, factors including body weight, physical activity, smoking, and breast reconstruction.

Methods

Study cohort: eligibility and ascertainment

Eligible women were residents of King County, Washington State, aged 21-74 years, who were diagnosed with a first primary invasive breast cancer between October, 2002 and July, 2004. Women were identified by the Cancer Surveillance System (CSS), a population-based registry operating as part of the SEER program of the U.S. National Cancer Institute. The study was

restricted to women who had had 5 or more lymph nodes removed during their breast cancer surgery; this served as an indicator of women who had likely undergone axillary dissection, as this information was not specifically available from the registry records.

Data collection: baseline and follow-up interviews

The study was approved by the Institutional Review Board of the Fred Hutchinson Cancer Research Center as well as the U.S. Department of Defense Human Subjects Committee. Women were invited to participate through a mailed letter of invitation that included a description of the study and interviewing procedures. A study interviewer then called potential participants, answered any remaining questions about the study, and, if a woman was willing, scheduled the baseline interview.

Baseline in-person interviews were conducted during the first 2.5 years of the 4-year study, with the goal of obtaining at least two follow-up interviews. The interview covered surgical, medical, and radiation treatments received; arm symptoms; medical history; lifestyle factors, including recreational activities, smoking, and alcohol consumption; reproductive history; and patient demographics. Similar information was collected during the follow-up interviews, focusing on the time period between interviews. In addition, at the second and third follow-up interviews, quality of life was assessed using the FACT-B (functional assessment of cancer therapy—breast) instrument.

Current weight and height were measured at the baseline interview. Also, at the baseline and follow-up interviews, each arm was measured using disposable paper tapes designed for this purpose (manufactured by Jobst, Inc.) To reduce the possibility that arm measurements could be

influenced by the presence of temporary post-operative swelling, baseline interviews were conducted at least 3 months after surgery (range, 4-32 months; median, 10 months).

In total, 443 women completed a baseline interview. Follow-up interviews were conducted at 6-9 month intervals throughout the study. At least one follow-up interview was obtained from 423 women, while 408 and 316 women, respectively, completed two or three follow-ups. One woman was later found to be ineligible (due to removal of <5 lymph nodes), and an additional nine were excluded from our analyses because they had had bilateral mastectomy and lymph node surgery, so that comparison of measured arm volume between the surgery side and unaffected side was not possible. Thus, the final study cohort was comprised of 433 women. Women were followed from 5-50 months after surgery (median, 32 months).

Outcome assessment and data analysis

We conducted separate analyses that identified lymphedema based either upon self-reported arm swelling or measured arm volume. To assess self-reported lymphedema, we asked women to report any difference between the size of their right and left arms or hands that persisted for more than two weeks. The date of self-reported lymphedema was the month and year that a woman had first noticed unilateral arm swelling on the surgery side. Lymphedema was also defined as a volume excess of 10% or greater of the surgery-side arm relative to the other arm, comparing measurements recorded for both arms on the same date. Arm volume was calculated using the formula for a truncated cone, using arm circumference measurements taken in a proximal direction from the wrist to axilla in 1.5 centimeter intervals, and hand circumference measurements taken distally from the wrist in 1.5 centimeter intervals.

Cox regression was used to estimate the relative risk of lymphedema and associated 95% confidence intervals for the exposures of interest. The time scale for all analyses was time since surgery. In the case of multiple cancer-related surgeries, the surgery date was the date in which axillary lymph nodes were removed. Women entered observation at the time of surgery and follow-up ended either at the time that arm swelling was first noticed (for analyses of self-reported lymphedema), or at the time that a 10% volume excess was first measured (for measured lymphedema) or at the time of the last interview (for women without lymphedema).

Exposure variables

Demographic characteristics and history of non-cancer medical conditions presented are based on data from the baseline interview. Cancer treatments, including chemotherapy, radiation, and tamoxifen, were assessed at each interview, and were treated as time-dependent variables in our analyses. Some other characteristics, including cigarette smoking, aspects of body size (assessed as body mass index (BMI) and as change in weight after cancer diagnosis), and physical activity were assessed both before and after breast cancer diagnosis.

Results

Occurrence of lymphedema

Slightly more than half of the study participants reported arm swelling (n=228; 52.7%). Of these, swelling was reported to have begun before the baseline interview by 153 women, of whom all but 7 indicated that swelling was still present at baseline. The onset of arm swelling was reported by an additional 32, 27, and 16 women at the first, second, and third follow-up interviews, respectively. Self-reported arm swelling began from 0-38 months after surgery (median, 6 months; mean, 9 months).

Arm volume excess of 10% or greater, comparing the surgery-side to the opposite arm, was identified in 73 women (16.9%). For one half of these women (n=36), the volume excess was first measured at the baseline interview, while 15, 10 and 12 additional women had 10% arm volume excess first measured at the first, second and third follow-up interviews, respectively. Sixty (82.2%) of the 73 women with lymphedema based on measurement reported arm swelling, and, of these, all but 6 noticed swelling before the increase in volume was measured. Of the 205 women who did not report arm swelling at any interview, a 10% volume excess was measured among 13 (6.3%).

Risk factors

We assessed risk factors for self-reported and measured lymphedema (10% volume excess) in separate analyses, both of which adjusted for time since surgery. Associations with demographic characteristics are presented in Tables 1 and 2. We observed no clear association of age, race, or educational attainment with either self-reported or measured lymphedema. Unmarried women were at a somewhat increased risk of measured lymphedema (RR=1.9, 95% CI 1.2-3.1), although this association was attenuated in analyses based upon self-report.

Associations with cancer treatments are shown in Tables 3 and 4. Self-reported lymphedema occurred more frequently among women who had had radiation treatment or chemotherapy, while no association with breast cancer surgery (lumpectomy vs. mastectomy), breast reconstruction, or tamoxifen use was observed. Risk of self-reported lymphedema also increased with increasing number of lymph nodes removed: relative to women with 5-9 nodes removed, risk was more than doubled among those with 20 or more nodes removed. In contrast, no statistically significant

association with any type of breast cancer treatment, or with number of nodes removed, was apparent in analyses of 10% measured increase in arm volume. Non-significant increases in risk of similar or lesser magnitude than those observed for self-reported lymphedema were observed in association with number of lymph nodes removed, radiation, and chemotherapy.

Associations with characteristics of women reported at the baseline interview are presented in Tables 5 and 6. Self-reported lymphedema occurred more commonly among women with greater BMI (e.g., RR= 1.6, 95% CI 1.2-2.1, for BMI $\geq$30 vs. BMI <25). No clear increases in risk of self-reported lymphedema were observed in association with smoking status at the time of cancer diagnosis, physical activity level, or medical conditions including hypertension and diabetes. In analyses of 10% measured arm volume excess, we also observed an association with increasing BMI (e.g., RR= 2.9, 95% CI 1.6-5.1, for BMI $\geq$30 vs. BMI <25). In addition, risk was increased among women who were current smokers at the time of cancer diagnosis, and among women with a history of hypertension. Risk was reduced among women who engaged in recreational physical activity during the two years prior to cancer diagnosis; e.g, among women who engaged in $\geq$ 4.7 hours per week, the RR was 0.4 (95 % CI, 0.2-0.8).

Associations with exposures and behaviors after breast cancer diagnosis are examined in Tables 7 and 8. We observed no indication that infection of the surgery-side arm increased risk of either self-reported or measured lymphedema. Performance of post-operative arm stretching exercises also was not associated with lymphedema. For self-reported lymphedema, we observed no association with either smoking or level of recreational physical activity after cancer diagnosis; however, risk was increased by 40-50% among women who experienced either a weight gain or loss of >10 pounds, relative to their weight before breast cancer diagnosis. These results contrasted

in several ways with our findings regarding 10% measured arm volume excess. For the latter definition of lymphedema, risk was increased among current smokers (RR=2.2, 95% CI 1.1-4.4) and reduced among women in the highest category of recreational physical activity. Also, no increase in risk was noted among women who reported weight gain after diagnosis, while women who lost >10 pounds were at increased risk.

Discussion

Relatively little research has been conducted on the etiology or prevention of lymphedema, yet many women are affected with this condition after treatment for breast cancer. Strengths of the current study include the use of standardized procedures for measurement of arm volume and structured questionnaires in the context of a prospective study. We restricted our study to women with 5 or more lymph nodes removed, as these women are thought to be at higher risk of subsequent lymphedema. Our study also had important limitations, chiefly the inability in our study setting to conduct arm measurements and baseline interviews before breast or axillary surgery was performed. Also, while self-reported arm swelling was commonly reported, only a relatively small number of women experienced an increase in arm volume (10%) that could be reliably ascertained through arm measurement. Thus, considerably larger studies will be needed to assess risks associated with measured arm volume with precision.

We observed increases in risk of self-reported lymphedema associated with some aspects of cancer treatment, including radiation treatment, chemotherapy, and number of lymph nodes removed. The strength of associations of measured lymphedema with most breast cancer treatments were fairly similar to those noted for self-reported lymphedema, although the precision of these estimates was reduced. Measured lymphedema was not associated with number of lymph nodes removed, in

contrast to our findings for self-report. It is possible that self-report of lymphedema may have been influenced by heightened risk awareness among women who had had more extensive axillary surgery; if so, the strength of association of number of lymph nodes removed with self-reported lymphedema may be falsely high.

Increasing body mass index at the time of cancer diagnosis was associated with an increased risk of both self-reported and measured lymphedema, with the association somewhat more evident for measured lymphedema. For a number of other characteristics, including smoking at the time of cancer diagnosis, reduced extent of recreational physical activity level during the two years prior to cancer diagnosis, and history of hypertension, an increased risk of measured, but not self-reported, lymphedema was observed.

Characteristics and behaviors that may be altered after breast cancer diagnosis might be expected to offer the most promise for development of novel lymphedema prevention strategies. We observed no evidence that the occurrence of arm infection after surgery, or the conduct of post-operative arm stretching exercises, were associated with either self-reported or measured lymphedema. Neither recreational physical activity nor cigarette smoking after cancer diagnosis were linked with self-reported lymphedema, while risk was moderately increased among women who either gained or lost weight after diagnosis. In contrast, risk of measured lymphedema was doubled among women who were current smokers after cancer diagnosis, and risk was reduced with increasing extent of recreational physical activity after diagnosis. Despite the finding that elevated BMI at cancer diagnosis was associated with an increased risk of measured lymphedema, no alteration in risk of measured lymphedema was noted among women who gained weight after diagnosis, while women who lost more than 10 pounds appeared to be at increased risk. These apparently contradictory

findings may reflect a higher pre-cancer BMI among women who lost weight after diagnosis, as we continued to observe an increased risk associated with greater BMI measured after diagnosis.

A majority of women who reported arm swelling first experienced this condition within 6 months of surgery, and before the baseline interview was conducted. Measured lymphedema (10% volume excess) occurred much less commonly than did self-reported swelling. Most women with measured lymphedema reported arm swelling before the volume excess was identified through measurement. Thus, measured lymphedema in this study tended to occur somewhat later, and may represent progression to more severe disease. It might be expected that lymphedema that develops shortly after initial treatment may be less amenable to risk reduction through behavioral alterations, and/or more likely to be influenced by breast cancer treatment. Our results offer some support for this hypothesis. We observed stronger associations of BMI (both before and after breast cancer diagnosis) with measured than with self-reported lymphedema. Also, we observed an increased risk of measured lymphedema with smoking after cancer diagnosis, and a reduced risk with increased levels of recreational physical activity; however, no associations with these characteristics were observed for self-reported lymphedema.

Our findings suggest that restraining from cigarette smoking, maintenance of normal (i.e., not overweight or obese) body mass, and participation in regular recreational physical activity should be investigated further as prevention strategies for lymphedema, particularly for lymphedema that develops some time after cancer treatment or progresses to more severe disease. These behaviors should be further investigated in randomized trials and in observational cohort studies. Such studies should be designed to enroll patients before cancer treatment is initiated, use objective

measures for determination of lymphedema, and be of sufficient size to allow the assessment of both moderate and severe disease.

Table 1. Risk of self-reported arm swelling associated with demographic characteristics

Characteristic	Women with swelling (n=228) n	%	RR[1]	95% CI
Age (years)				
<40	25	11.0	1.0	Ref
40-49	71	31.1	0.9	0.6-1.5
50-59	89	39.0	1.1	0.7-1.7
60+	43	18.9	0.7	0.4-1.1
Race				
white	185	81.1	1.0	Ref.
black	19	8.3	1.3	0.8-2.1
other	24	10.5	1.0	0.6-1.5
Education				
high school or less	33	14.5	1.0	Ref.
technical school or some college	89	39.0	1.0	0.7-1.6
college graduate	106	46.5	1.0	0.7-1.5
Marital status				
married	154	67.5	1.0	Ref.
single	74	32.5	1.2	0.9-1.6
Household income				
<50,000	88	38.6	1.0	Ref.
50,000-89,999	65	28.5	0.8	0.6-1.1
≥ 90,000	61	26.8	0.9	0.6-1.2
missing	14	6.1		

1. Relative risk adjusted for time since surgery.

Table 2. Risk of lymphedema (defined as 10% volume excess of surgery-side arm relative to other arm) associated with demographic characteristics

Characteristic	Women with swelling (n=73) n	%	RR[1]	95% CI
Age (years)				
<40	7	9.6	1.0	Ref.
40-49	20	27.4	1.0	0.4-2.3
50-59	27	37.0	1.1	0.5-2.5
60+	19	26.0	1.3	0.6-3.2
Race				
white	61	83.6	1.0	Ref.
black	7	9.6	1.3	0.6-2.9
other	5	6.8	0.6	0.3-1.6
Education				
high school or less	15	20.5	1.0	Ref.
technical school or some college	22	30.1	0.5	0.3-1.1
college graduate	36	49.3	0.8	0.4-1.4
Marital status				
married	41	56.2	1.0	Ref.
single	32	43.8	1.9	1.2-3.1
Household income (dollars)				
<50,000	36	49.3	1.0	Ref.
50,000-89,999	15	20.5	0.5	0.3-0.9
$\geq$ 90,000	16	21.9	0.6	0.3-1.1
missing	6	8.2		

1. Relative risk adjusted for time since surgery.

Table 3. Risk of self-reported arm swelling associated with breast cancer treatments received

Cancer treatment	Women with swelling (n=228) n	%	RR[1]	95% CI
Breast cancer surgery				
lumpectomy	107	46.9	1.0	Ref.
mastectomy	121	53.1	1.1	0.9-1.4
Number of lymph nodes removed				
5-9	54	23.7	1.0	Ref.
10-19	119	52.2	1.8	1.3-2.5
20+	55	24.1	2.3	1.5-3.3
Radiation				
no	127	55.7	1.0	Ref.
yes	101	44.3	1.3	1.0-1.8
Chemotherapy				
no	52	22.8	1.0	Ref.
yes	176	77.2	1.7	1.2-2.4
Tamoxifen				
no	186	81.9	1.0	Ref.
yes	41	18.1	1.0	0.7-1.4
missing	1			
Breast reconstruction				
no	217	95.2	1.0	Ref.
yes	11	4.8	1.1	0.6-2.0

1. Relative risk adjusted for time since surgery.

Table 4. Risk of lymphedema (defined as 10% volume excess of surgery-side arm relative to other arm) associated with breast cancer treatments received

Cancer treatment	Women with swelling (n=73) n	%	RR[1]	95% CI
Breast cancer surgery				
lumpectomy	30	41.1	1.0	Ref.
mastectomy	43	58.9	1.4	0.9-2.2
Number of lymph nodes removed				
5-9	20	27.4	1.0	Ref.
10-19	38	52.1	1.3	0.8-2.2
20+	15	20.5	1.3	0.6-2.5
Radiation treatment				
no	19	26.0	1.0	Ref.
yes	54	74.0	1.4	0.8-2.3
Chemotherapy				
no	9	12.3	1.0	Ref.
yes	64	87.7	1.6	0.8-3.3
Tamoxifen				
no	53	72.6	1.0	Ref.
yes	20	27.4	0.8	0.4-1.3
Breast reconstruction				
no	70	95.9	1.0	Ref.
yes	3	4.1	0.5	0.2-1.6

1. Relative risk adjusted for time since surgery.

Table 5. Risk of self-reported arm swelling associated personal characteristics prior to breast cancer diagnosis or baseline interview

Characteristic	Women with swelling (n=228) n	%	RR[1]	95% CI
Body mass index (1 month before cancer diagnosis)				
<25	86	57.9	1.0	Ref.
25-<30	68	30.3	1.3	0.9-1.8
30+	73	11.8	1.6	1.2-2.1
missing	1			
Smoking during the year before cancer diagnosis				
never	132	57.9	1.0	Ref.
former	69	30.3	1.1	0.8-1.5
current	27	11.8	0.9	0.6-1.3
Dominant arm				
not surgery side	113	52.1	1.0	Ref.
surgery side	104	47.9	1.0	0.8-1.3
missing	11			
Recreational physical activity (in 2 yrs before diagnosis)				
none	29	12.7	1.0	Ref.
>0-<1.9 hours per week	65	28.5	1.2	0.8-1.9
1.9-<4.7 hours per week	71	31.1	1.2	0.8-1.9
≥4.7 hours per week	63	27.6	1.1	0.7-1.7
History of hypertension (before baseline interview)				
no	163	71.5	1.0	Ref.
yes	65	28.5	1.2	0.9-1.6
History of diabetes (before baseline interview)				
no	214	93.9	1.0	Ref.
yes	14	6.1	1.1	0.6-1.9

1. Relative risk adjusted for time since surgery.

Table 6. Risk of lymphedema (defined as 10% volume excess of surgery-side arm relative to other arm) associated with personal characteristics prior to breast cancer diagnosis or baseline interview

Characteristic	Women with swelling (n=73) n	%	RR[1]	95% CI
Body mass index (1 month before cancer diagnosis)				
<25	19	26.8	1.0	Ref.
25-<30	20	28.2	1.7	0.9-3.1
30+	32	45.1	2.9	1.6-5.1
missing	2			
Smoking during the year before cancer diagnosis				
never	40	54.8	1.0	Ref.
former	18	24.7	0.9	0.5-1.5
current	15	20.5	1.7	1.0-3.1
Dominant arm				
not surgery side	37	56.9	1.0	Ref.
surgery side	28	43.1	0.8	0.5-1.3
missing	8			
Recreational physical activity (in 2 yrs before diagnosis)				
none	16	21.9	1.0	Ref.
>0-<1.9 hours per week	21	28.8	0.6	0.3-1.2
1.9-<4.7 hours per week	23	31.5	0.7	0.4-1.3
≥4.7 hours per week	13	17.8	0.4	0.2-0.8
History of hypertension (before baseline interview)				
no	43	58.9	1.0	Ref.
yes	30	41.1	2.1	1.3-3.4
History of diabetes (before baseline interview)				
no	66	90.4	1.0	Ref.
yes	7	9.6	1.7	0.8-3.8

1. Relative risk adjusted for time since surgery.

Table 7. Risk of self-reported arm swelling associated with exposures and behaviors after breast cancer diagnosis

Characteristic	Women with swelling (n=228) n	%	RR[1]	95% CI
Smoking after diagnosis				
not current	216	94.7	1.0	Ref.
current	12	5.3	0.7	0.4-1.3
Body mass index after diagnosis				
<25	58	29.4	1.0	Ref.
25-<30	71	36.0	1.6	1.2-2.3
30+	68	34.5	1.6	1.1-2.2
missing	31			
Weight change after diagnosis				
≤ 10 pounds	109	54.2	1.0	Ref.
> 10 pound gain	59	29.4	1.4	1.0-2.0
> 10 pound loss	33	16.4	1.5	1.0-2.2
	27			
Recreational physical activity after diagnosis				
none	38	16.7	1.0	Ref.
>0-<1 hours per week	61	26.7	0.8	0.5-1.2
1-<2.9 hours per week	74	32.5	1.0	0.7-1.5
≥2.9 hours per week	55	24.1	0.8	0.5-1.1
Infection of surgery side arm after cancer diagnosis				
no	220	96.5	1.0	Ref.
yes	8	3.5	0.9	0.4-1.7
Post-operative arm-stretching exercises				
no	112	49.1	1.0	Ref.
yes	116	50.9	0.9	0.7-1.2

1. Relative risk adjusted for time since surgery.

Table 8. Risk of lymphedema (defined as 10% volume excess of surgery-side arm relative to other arm, developing after the baseline interview) associated with exposures and behaviors after breast cancer diagnosis

Characteristic	Women with swelling (n=73) n	%	RR[1]	95% CI
Smoking after diagnosis				
not current	64	87.7	1.0	Ref.
current	9	12.3	2.2	1.1-4.4
Body mass index after diagnosis				
<25	16	23.9	1.0	Ref.
25-<30	21	31.3	1.7	0.9-3.3
30+	30	44.8	2.3	1.2-4.3
missing	6			
Weight change after diagnosis				
≤ 10 pounds	35	51.5	1.0	Ref.
> 10 pound gain	16	23.5	1.0	0.5-1.7
> 10 pound loss	17	25.0	2.3	1.3-4.2
	5			
Recreational physical activity after diagnosis				
none	16	21.9	1.0	Ref.
>0-<1 hours per week	23	31.5	0.8	0.4-1.5
1-<2.9 hours per week	23	31.5	0.8	0.4-1.5
≥2.9 hours per week	11	15.1	0.4	0.2-0.8
Infection of surgery-side arm after cancer diagnosis				
no	70	95.9	1.0	Ref.
yes	3	4.1	0.7	0.2-2.1
Post-operative arm-stretching exercises				
no	33	45.2	1.0	Ref.
yes	40	54.8	1.1	0.7-1.7

1. Relative risk adjusted for time since surgery.